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A CLASSIFICATION OF NERVE INJURIES

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In 1863, during the fiercest days of the American Civil War, Dr. W. A. Hammond, Surgeon-General to the Federal Armies, ordered the establishment of a unit for the observation and treatment of injuries of the nervous system. A signal result of this instruction was the appearance in 1864 of a little book by Weir Mitchell, Morehouse, and Keen, *Gunshot Wounds and Other Injuries of Nerves.* This gave an account of the first organized study of nerve injuries, and in it we find not only the most perfect description of causalgia, a condition that will always remain associated with the name of Weir Mitchell, but descriptions of nerve injuries as we see them to-day. These enthusiastic workers laid a good foundation for all that has followed during the succeeding 80 years. But the means of investigation at their disposal were very limited, open operations were rare, and the syndromes described are not quite sufficiently clear-cut to serve as a guide in diagnosis and prognosis.

The enormous number of nerve injuries dealt with during the last war gave to neurologists and surgeons a very clear conception of the results of division of a nerve, but one gets the impression that they were so preoccupied with the repair of nerves so seriously damaged as to require resection and suture that there was hardly time to investigate the great mass of cases in which something less than complete division was present, cases in which spontaneous recovery usually occurred. So far as nerve injuries are concerned this war has been more leisurely.

It is the purpose of this preliminary communication to describe three well-defined types of nerve injury, types so distinctive that it has been found convenient, and indeed necessary, to apply labels to them and make them the basis for a clinico-pathological classification. It might be foolish to claim that every nerve injury can be fitted into this classification, but from the study of 460 cases at the Oxford Centre it has become evident that the majority can be so classified provided one realizes that a combination of lesions is not infrequently present as the result of a single injury.

Clinical Signs of Damage

The clinical manifestations of damage to a peripheral nerve may be considered under two headings.

1. *Those due to Loss of Function:*—
   Efferent: Paralysis of muscles; sudomotor paralysis; pilomotor paralysis; vasomotor paralysis.
   Afferent: Loss of tactile sensibility; loss of pain sensibility; loss of thermal sensibility; loss of joint and postural sensibility; loss of deep sensibility.
2. *Those due to Perversions of Function:*—
   Efferent: Muscle twitching (fasciculation); muscle spasm; abnormal sweating; vasomotor disturbances.
   Afferent: Paraesthesia; apparently spontaneous pain, and pain quite outside the range of normal experience; abnormal responses to heat and cold.

In contemporary clinical practice there is no question whatever that in frequency and importance the first group of phenomena far outweigh the second, and it is with loss of function alone that this classification is concerned.

Although, as has been said, there is a fairly clear understanding among clinicians and experimental workers about the sequence of events following complete anatomical division of a peripheral nerve, there is considerable confusion when we come to examine those numerous cases in which function is lost although anatomical continuity of the nerve is more or less preserved. No clear distinction has been drawn between those intraneural lesions that are followed by complete peripheral degeneration and those in which the rate of recovery is so rapid that degeneration could not possibly have occurred. The well-known term "physiological interruption" conjures up no clear pathological picture, and it is inaccurate in that no interruption of conductivity can properly be called physiological. Similarly, the terms "concussion," "compression," and "contusion" are equally vague; for although they may give a hint of the nature of the cause they do not describe the effect of the injury on the nerve itself.

At a meeting of the Association of Physicians held in April, 1941, I propounded the following classification:

1. Complete anatomical division of a nerve.
2. A "lesion in continuity," in which more or less of the supporting structure of the nerve is preserved but there is nevertheless such disturbance of the nerve fibres that true Wallerian degeneration occurs peripherally.
3. "Transient block."—A minimal lesion producing paralysis that is incomplete more often than not; it is unaccompanied by peripheral degeneration and recovers rapidly and completely.

These three syndromes are well known to neurologists, and discussion centred chiefly on terminology. It may be argued with justification that "lesion in continuity" is ambiguous and might well include "transient block"; for there is no doubt that in transient block the nerve is in continuity. It was therefore suggested by Prof. Henry Cohen that distinctive names should be given to these three types of nerve injury so that confusion might be avoided. He writes:

"Etymologically these words indicate the ideas they are intended to convey, and they have not previously been used—so that the field for them is clear.

"1. *Neurotmesis* (τμῆσις, a 'cutting' which implies a separation of related parts), which describes the state of a nerve that has been completely divided. The injury produces a lesion which is in every sense complete.

"2. *Axonotmesis:* Here the essential lesion is damage to the nerve fibres of such severity that complete peripheral degeneration has followed; and yet the sheath and the more intimate supporting structures of the nerve have not been completely divided, which means that the nerve as a mass of tissue is still in continuity.

"3. *Neurapraxia* (ἀπραξία, non-action) is used to describe those cases in which there is a short-lived paralysis—so short that recovery could not possibly be explained in terms of true regeneration."

The classification is partly morphological, though in each case the clinical behaviour is characteristic. The three types of lesion have been produced experimentally, and work of this kind has contributed considerably to our understanding of them.

It is not proposed here to give more than an outline of the characteristics of the three types, since full descriptions will be published shortly (by me, on neurotmesis, axonotmesis, and neurapraxia; and by W. B. Highet on mixed and incomplete lesions, which are grouped together as *dissociated* paralyses). The classification is presented in brief in the hope that it will prove helpful to clinicians in sorting out their cases of nerve injury.

Neurotmesis (Division of a Nerve)

The clinical and pathological picture presented by complete division of a nerve is so familiar that no more than the briefest description is necessary. At the *site of damage* a swelling which is called a "neuroma" appears at the end of the central stump; it consists of a mass of scar tissue and new nerve fibres in no way different from what is seen in an amputation neuroma. The swelling is sometimes palpable and tender. A swelling also appears at the end of the peripheral stump; it is called a "glioma," is composed of Schwann cells and fibrous tissue, is much smaller than the neuroma, and is rarely palpable clinically.

In the *distribution of the nerve* there is complete sensory and motor paralysis; the affected muscles degenerate and waste, and respond to electrical stimulation with the characteristic reaction of degeneration. The only difficulties in diagnosis are anatomical—in cases where some anomaly in distribution may lead the clinician to believe that the lesion is an incomplete one.

For all practical purposes recovery never occurs in the absence of surgical repair. If suture is followed by regeneration, signs of recovery appear in anatomical order; this is best seen on the motor side, where a regular march of recovery in muscles is often observed. The quality of recovery is always short of perfect, not only because of irreversible degenerative changes in end-organs and muscle but because of confusion at the suture line.

Axonotmesis (Lesion in Continuity)

If a nerve is crushed heavily with forceps all the nerve fibres are broken, but the connective tissue of the nerve survives to some extent; although the gap in the nerve fibres may be quite noticeable at first it is followed by a flowing together of the fibre protoplasm above and below, so that when observed a few minutes after removal of the instrument the lesion, which at first was nothing more than a thin ribbon of connective tissue joining central and peripheral stumps, has filled out to almost normal diameter. There is probably no case in which the connecting function of connective tissue is of greater importance; for it is found that, although the peripheral stump degenerates completely, spontaneous regeneration invariably follows after such an experimental lesion.

Now, it often happens that a nerve is damaged in a somewhat similar way by a "near miss," or pressure from one of the fragments of a fractured bone—in fact, by any injury that fails to divide the nerve completely. It is not to be expected that the accidents of daily life or warfare produce lesions as uniform as those produced in the laboratory: the nature and degree of violence are variable, and so is the extent of the damage done. The lesion exposed at operation may be the familiar fusiform neuroma or nerve spindle: more frequently (as in the experimental lesion) there is little to see beyond slight swelling or constriction, perhaps perineural adhesions and a little thickening of the epineurium. However, in general, the behaviour of lesions of this type is characteristic. The lesion is called "axonotmesis" because its essential feature is complete interruption of nerve fibres with preservation of more or less of the supporting structure of the nerve. After a period of several weeks or a few months new fibres manage to make their way through the scar tissue at the site of the lesion, and regeneration then proceeds in an anatomically orderly fashion down the peripheral stump. In experimental animals (rabbits) the rate of regeneration is faster after axonotmesis than after neurotmesis, but we are not yet sure that this is the case in man, although there is some evidence to suggest it. What is quite certain is that functional recovery is far better, and it is reasonable to suppose that this is due to the growth of fibres into their old pathways; some of them may go astray, but the majority are guided by the endoneurium and perineurium into their old channels. Everyone is familiar with the excellent spontaneous recovery that generally follows radial paralysis complicating fractures of the humerus, and this is the best example of axonotmesis in clinical practice.

It cannot be emphasized too strongly that there is no clinical difference whatever between the paralysis resulting from axonotmesis and that following neurotmesis. Seeing that peripheral degeneration is complete one could not possibly expect to find any, and indeed there is none. How, then, are the two conditions to be distinguished? There are three possible ways.

Experience teaches us that certain injuries are likely to cause neurotmesis, while others are more likely to cause axonotmesis. Radial paralysis complicating a gunshot wound of the arm is likely to be due to neurotmesis, in which case recovery will not occur unless the nerve is sutured. On the other hand, a closed fracture of the humerus involving the radial nerve almost always produces axonotmesis: by the time treatment of the fracture is completed there is generally some sign of recovery. On can therefore make a shrewd guess from knowledge of the nature of the injury. The second way is to wait until sufficient time has elapsed for spontaneous regeneration to occur. If signs of recovery fail to appear, then neurotmesis may be suspected and the nerve should be explored. This has been the general policy in the past, but the time of waiting has been too long; it is clear that if the lesion is in fact neurotmesis valuable months will have been wasted. No harm comes from exploring a nerve, and it has become our practice to carry out exploration in every case in which regeneration has not appeared within the calculated time.* This brings us to the third and only precise method—i.e., exploration. Riddoch has repeatedly emphasized that we should regard operative exposure of the lesion as a necessary step in the establishment of the diagnosis. Provided that the operation is carried out by a competent surgeon who is familiar with every detail of the neurological picture, and provided his approach to the nerve lesion itself is conservative rather than radical, exploration is a commendable procedure. It may reveal a somewhat unexpected neurotmesis; it may reveal axonotmesis, in which case the surgeon and the patient know what to expect—i.e., spontaneous regeneration.

Neurapraxia (Transient Block)

Recovery from certain nerve injuries is remarkably rapid—indeed, so speedy that it cannot possibly be explained in terms of axonal regeneration. Lesions of this type, like axonotmesis, may be produced by any injury that does not actually sever the nerve, but the violence is not of a high order. Tourniquet paralysis, Saturday-night paralysis, crutch paralysis, are all familiar examples—though sometimes these injuries may be sufficient to produce true degenerative changes.

Since the condition is essentially a clinical syndrome it is best to describe its clinical characteristics first: (*a*) the paralysis is predominantly motor; (*b*) there is little wasting; the electrical reactions of the muscle persist unchanged; (*c*) subjective sensory disturbances—numbness, tingling, pins-and-needles, burning—are common; (*d*) objective sensory disturbances are generally partial, often minimal, so far as touch, pain, heat, and cold are concerned; (*e*) loss of postural sensibility and vibration sense are common; (*f*) loss of sweating is unusual. Muscle tone is said to be retained, but this has not been our experience.

It is clear, then, that the lesion is a dissociated one: the motor and proprioceptive fibres suffer more than those subserving other functions, and there is a physiological explanation for this. Recovery, which can be predicted with absolute confidence if examination reveals this syndrome, is fairly rapid, beginning usually after two to three weeks and complete within six to eight—though I have seen a few cases in which complete restoration of function was delayed until the fourth month. The progress of recovery is irregular;

* A paper dealing with rates of regeneration will be published within the next few months.

it follows no anatomical order—it may appear suddenly throughout the whole distribution of the affected nerve, and resembles nothing so much as the wearing off of the effects of local anaesthesia. In the few cases in which it is delayed it is still much more rapid than the fastest recovery from axonotmesis, and would demand a rate of growth of axons quite unknown in clinical or laboratory experience. Furthermore, the preservation of normal excitability of muscles is clear evidence against Wallerian degeneration of the nerve below the lesion, and we now have evidence on the motor side that the affected nerve is not only capable of conducting impulses but in fact does so, though no contraction of the muscle can be detected clinically. There is therefore a disturbance of conduction (which can be produced experimentally) that impedes the transmission of impulses but does not destroy the axon. Recovery is always perfect.

Neurapraxia is a non-committal but adequate description of this non-functioning of a nerve. Neurapraxia is produced by cocainization of a nerve, by mild degrees of refrigeration, and by slight injury.

Comment

It is obvious that by no means all nerve injuries can be classified under these simple headings; the accidents that produce them are not uniform in their effects unless the violence is great. An injury may affect the fibres of a nerve in varying degree, and the clinical picture will then be more complex. A lesion may be made up by a combination of any of the following: (*a*) neurotmesis; (*b*) axonotmesis; (*c*) neurapraxia; (*d*) normal fibres.

Indeed, neurapraxia is a lesion in which a certain number of normally functioning fibres are always present. Leaving this aside, there are no fewer than eleven possible combinations of these lesions, each with its own clinical characteristics! In complicated lesions of the brachial plexus, for example, the picture may be so mixed that precise diagnosis is impossible, though there is often plenty of scope for light-hearted speculation. We have seen almost every one of the possible combinations, and do claim that none of the phenomena of interruption of a nerve that we have so far encountered required other explanation. This is a very difficult field of clinical inquiry, and it is not proposed to discuss it here, seeing that the various combinations of lesions form the subject of a paper that will shortly be published by W. B. Highet, who has investigated all the cases of dissociated paralysis seen at the Oxford Centre since its inception in June, 1940.

CAROTINAEMIA

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We have recently observed 5 cases showing pigmentation of the skin pronounced enough to warrant provisional diagnoses, by the attending practitioners, of "jaundice," "pernicious anaemia," "haemolytic anaemia," and "cholelithiasis." This pigmentation can only be properly described as "carroty," and while in the mild cases it is most obvious in the naso-labial folds and the palms of the hands, in the more advanced cases it is a generalized body tanning. The condition is due to the excessive consumption of carrots, though it has been recorded when other lipochrome foods are eaten in quantity.

The Literature of Carotinaemia

The term "carotinaemia" for the orange pigmentation of the skin observed after the excessive consumption of carrots and other vegetables was first applied by Hess and Myers in 1919. The observation of this skin discoloration in diabetics whose diet consisted mainly of foods rich in yellow lipochrome—fruit, vegetables, butter, and eggs—was made by von Noorden (1907), who considered the condition to be a diabetic manifestation. Moro (1908) noted that normal infants developed a similar pigmentation when carrots were added to the diet. Van den Bergh and Snapper (1913) showed that there were lipochrome pigments circulating in the blood of diabetic patients with the orange pigmentation, and that these pigments were identical spectroscopically with those of carrots and other vegetables. Salomon (1919) referred to this pseudo-icterus in non-diabetic patients whose diet largely consisted of the foods mentioned, and the gradual disappearance of this pigmentation with abstinence from such foods. Stoeltzner (1919), commenting on Kaupe's observation (1919) that nurslings lost their yellow coloration when their high carrot diet was stopped, observed that the number of similar children had increased during the last war. He called it a "pseudo-icterus" and thought a high tomato diet might produce a similar pigmentation.

Greene and Blackford (1926) and Stoner (1928) discussed the condition under the heading of "carotinaemia." Boeck and Yater (1929) used the term "xanthaemia" for the circulation in the blood of lipochrome pigments (thereby excluding bile pigments) and "xanthosis" for the visible presence of these yellow pigments in the skin. They found xanthaemia in all their nephritics and in most diabetics, and even in most "normal" cases examined. However, xanthosis was present in only 10% of the renal and diabetic cases and in only 3% of other cases. All these patients with stained skin had eaten excessively of lipochromic foods.

Stannus (1929) called the discoloration "hyperlipochromia," and concluded that it resulted from the failure to oxidize the carotinoid pigments in the body. He first reported carotinaemia in myxoedema, and Wendt (1935) noted the condition in some cretins. Bomford (1938) confirmed the presence of carotinaemia in some cases of myxoedema on a normal diet. On thyroid medication the lipochrome index fell to normal. He remarks that as the colour of cream is due to lipochromes, the description of the myxoedematous facies as a "strawberry and cream" complexion is not without justification.

The Present Series of Cases

Our interest in carotinaemia was first aroused by the visit of a clerk's wife on account of "jaundice," though her sclera was contrastingly white. In the spring months further cases were referred as "pernicious anaemia" and "haemolytic anaemia"; the woman with "gall-stones" was visiting her husband, an in-patient with acute nephritis, when the ward sister drew our attention to her carroty complexion. None of these patients had symptoms of ill-health, though the curious discoloration was a source of anxiety.

Careful histories were extracted to find the actual pounds of carrots consumed per week (see Table). As kitchen standards of quantity are given vaguely in pinches, spoons, and cups, we sought and obtained the number and size of the carrots, from which a correct estimate was made. These weights apply only to the raw carrots, as the other vegetables and cooked carrots were always eaten in pre-war helpings. During the

Table showing Amount of Carrots consumed Weekly

Occupation of Husband	Provisional Diagnosis (own Doctor)	Raw Carrots		Other Veg. and Eggs	Icteric Index	Serum Bilirubin (mg./100 c.cm.)	On Normal Diet Fading		Other Medical Conditions
		lb. per Week	Threshold Months				First Noticed (Weeks)	Complete (Weeks)	
Lorry-driver	Gall-stones	8	8	—	10	0·1	3	6	Cholecystectomy, 1932
Clerk ..	Jaundice	6	6	+++	8	0·3	2	4	Microcytic anaemia
Shop-keeper	Pernicious anaemia	5	7	+	12	0·6	2	4	Mitral stenosis
Corporal	Haemolytic anaemia	4	8	+	8	0·1	2	5	Microcytic anaemia
Baby ..		breast-fed	2	—	—	—	4	8	Healthy